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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/549,665

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Adrian Merlo

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03/20/2009

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EXAMINER

SCHLIENTZ, LEAH H

ART UNIT

PAPER NUMBER

1618

MAIL DATE

DELIVERY MODE

03/20/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/549,665	Applicant(s) MERLO ET AL.	
	Examiner Leah Schlientz	Art Unit 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 February 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 and 17-30 is/are pending in the application.
- 4a) Of the above claim(s) 1-13 and 21-28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 17-20, 29 and 30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

Applicant's election of Group II, claims 17-20, 29 and 30 in the reply filed on 2/19/2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The election of the following species is also acknowledged: ^{111}In -DOTA-[Thi⁸,Met(O₂)¹¹]-Substance P. Applicant's request that claims 21-28 be considered along with the elected claims has been considered. However, the examiner respectfully submits that the claims are distinct from the elected species, for reasons set forth in the Requirement for Restriction mailed 1/27/09.

Status of Claims

Claims 1-13 and 17-30 are pending, of which claims 1-13 and 21-28 are withdrawn from consideration at this time as being drawn to a non-elected invention. Claims 17-20, 29 and 30 are readable upon the elected invention and species, and are examined herein on the merits for patentability.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29 and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are rejected as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: e.g. method steps, such as conjugating a substance P analogue to a chelator molecule.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

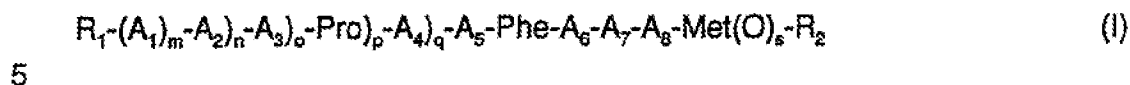
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17-20, 29 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Visser *et al.* (WO 92/18536).

Visser discloses methods for detecting and localizing tissues having neurokinine 1 receptors in the body of a warm-blooded living being by administration of a labeled small peptide having selective affinity to neurokinine 1 receptor, and by then radioassaying said being. The method also relates to therapeutic treatment of tumors (abstract). Diagnosis and therapy of gliomas are disclosed (page 1, lines 29+). A peptide having an affinity for neurokinine 1 receptors is labeled with (a) a detectable metal isotope selected from the group consisting of In-111, etc., said metal isotope being attached to said peptide via a suitable linker capable of reacting with an amino

Art Unit: 1618

group, preferably a terminal amino group of said peptide, and having a chelating group for chelating said metal isotope (page 2, lines 19-28). The labeled peptide is derived from the following formula (page 4), including substance p and derivatives thereof in examples 1-5:



- 5 wherein all of the symbols m, n, o, p and q are 1, or all but one of the symbols m, n, o, p and q are 1 and the remaining symbol is 0;
 R_1 is a hydrogen atom or a C_1 - C_4 alkylcarbonyl group;
 R_2 is an amino group, a hydroxy group or a C_1 - C_4 alkoxy group;
 10 A_1 is Arg, Gly or 5-oxo-Pro (pGlu);
 A_2 is Pro or β -Ala;
 A_3 is Lys or Asp;
 A_4 is Gln, Asn or 5-oxo-Pro;
 A_5 is Gln, Lys, Arg, N-acylated Arg or 5-oxo-Pro;
 15 or wherein A_5 together with A_3 forms a cystine moiety;
 A_6 is Phe or Tyr;
 A_7 is Gly, Ser or Pro;
 A_8 is Leu or Pro; and
 s is 0, 1 or 2;
 20 or a Tyr^o derivative thereof.

A suitable linker for attaching a metal isotope to the small peptide is provided with a chelating group, e.g. DOTA, etc (page 5, line 30-page 6, line 35).

Pharmaceutical compositions including carrier, etc. are disclosed (page 7, lines 1-11).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

Art Unit: 1618

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148

USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 17-20, 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Visser *et al.* (WO 92/18536) in view of Coy *et al.* (US 5,750,646).

Visser discloses radiolabelled chelator-substance p analogue conjugates for diagnosis and therapy of tumor displaying neurokinine 1 receptors, as set forth above.

Visser does not specifically recite substitution of Thi for Phe at position 8 of the instantly claimed amino acid sequence. Rather, Visser teaches Phe or Tyr at this position (A₆ in the notation of Visser).

However, nonnatural amino acids such as thienylalanine are known in the art to be interchangeable with Phe in similar peptide systems as shown by Coy.

Coy discloses linear peptides which are analogues of naturally occurring biologically active peptides having an active site and a binding site responsible for binding of the peptide to a receptor on a target cell (see abstract). Substance P and related peptides are disclosed (see column 20 and Table 1). A bradykinin antagonist of

Art Unit: 1618

formula $Q^0-A^1-A^2-A^3-A^4-Gly-A^5-A^6-A^7-A^8-A^9-Z^{10}$ is disclosed, wherein A^8 is Phe, p-X-Phe, or thienylalanine (see claim 1).

It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute Thi for Phe at position 7 and/or 8 of the substance P analogue-chelators disclosed by Visser. The Supreme Court in *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, 82 USPQ2d 1385, 1395-97 (2007) identified a number of rationales to support a conclusion of obviousness which are consistent with the proper “functional approach” to the determination of obviousness as laid down in *Graham*. One such rationale includes the simple substitution of one known element for another to obtain predictable results. The key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. See MPEP 2143. In the instant case, the substituted components (Thi and Phe) and their functions were known in the art at the time of the instant invention. For example, Coy teaches Phe and Thi to be interchangeable as a given residue in bradykinin antagonist peptides. One of ordinary skill in the art could have substituted one known amino acid for another, and the results of the substitution would have been predictable, that is a biologically active peptide having an active site and a binding site responsible for binding of the peptide (substance p analogue) to a receptor (e.g. neurokinine 1 receptor), especially as Coy is concerned with maintaining binding as in the naturally occurring peptide (abstract).

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

LHS